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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/419,901	10/18/1999	JENNIFER E. VAN EYK	PTQ-0028	2043

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LICATA & TYRRELL P.C.
66 E. MAIN STREET
MARLTON, NJ 08053

EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

NOTIFICATION DATE	DELIVERY MODE
08/07/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

poreilly@licataandtyrrell.com

Office Action Summary	Application No.	Applicant(s)	
	09/419,901	VAN EYK ET AL.	
	Examiner	Art Unit	
	LISA V. COOK	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,16-18,20-27,31,34,35 and 37-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 16-18, 20-27, 31, 34-35, and 37-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/20/08 has been entered.

Amendment Entry

2. Applicant's response to the Office Action mailed November 30, 2007 is acknowledged (paper filed 5/20/08). Claims 8-15, 19, 28-30, 32-33, 36, and 42-68 have been canceled. Currently claims 1-7, 16-18, 20-27, 31, 34-35, and 37-41 are pending and under consideration.

3. Objections and/or rejections of record not reiterated below have been withdrawn.

NEW GROUNDS OF REJECTIONS NECESSITATED BY AMENDMENT

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 1, 16-18, 20-27, 31 and 34 are rejected under 35 U.S.C.103 (a) as being unpatentable over Takahashi et al. (Clinical Biochemistry, Volume 29, No.4, August 1996, pages 301-308) in view of Solaro et al. (Journal of Molecular Cell Cardiology, Vol.28, pages 217-230, 1996) and Lin et al. (The journal of Biological Chemistry, Vol.271, No.1, 1/5/1996, pages 244-249) and further in view of Han et al. (International Journal of Biochemistry, Vol.24, No.1, 1992, pages 19-28).

Takahashi et al. teach method for measuring skeletal troponin I (fsTnI) in skeletal muscle damage. See abstract. The developed ELISA assay for fsTnI was specific for that isoform, and was used to determine the serum levels of fsTnI in healthy subjects and various forms of skeletal muscle damage. The serum level of fsTnI in healthy subjects was very low. This indicated that minor elevation of fsTnI could prove diagnostic for skeletal muscle damage. see page 305, 2nd column - Discussion.

Takahashi et al. differ from the instant invention in not specifically teaching myofilament protein modification products.

The specification has indicated that phosphorylation is a process resulting in myofilament protein modification products. See page 10 lines 10-24 for example.

Solaro et al. teach that myofilament proteins are important in the change of cardiac function associated with ischemia, reperfusion injury, and stunning – muscle damage. See page 227, 1st column–Conclusion. The mechanical state of the myofilament proteins by covalent, non-covalent, and the isoform population are involved in the transition from diastolic to the systolic state. See abstract. The myofilament proteins include actin, TnC, TnI, and Tm. See figure 1 on page 218.

Myofilament phosphorylation is also taught to be important in the interaction of TnI/TnC and relaxation rates due to calcium sensitivity. See page 221 - 1st and 2nd column/figure 3. TnI residue (myofilament protein modification products) phosphorylation has important effects on the interaction of TnI with TnC which can lead to reduced sensitivity of the myofilaments to Ca2+ and increased relaxation rated of the myofilaments. See page 221.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to measure myofilament protein modification products as taught by Solaro et al. in the muscle assessment methods of Takahashi et al. because Solaro et al. taught that TnI residue (myofilament protein modification products) phosphorylation has important effect on the interaction of TnI with TnC which can lead to reduced sensitivity of the myofilaments to Ca2+ and increased relaxation rated of the myofilaments. See page 221. Such altered myofilament functions could lead to cardiac injury, damage and or death. See page 222.

Takahashi et al. in view of Solaro et al. differ from the instant invention in not specifically detecting a chemical adduct of the myofilament protein modification product.

However, Lin et al. teach procedures to measure covalent binding of peptides to cardiac troponin C. Troponin C is disclosed as important in the regulation of contraction in striated muscle. In order to test troponin C's involvement in muscle contraction, a synthetic peptide or biotin was coupled to troponin to produce covalent adducts.

These adducts were evaluated for activity in TnC-extracted myofibrils. See abstract and page 244-2nd column 3rd paragraph and figure 4. In some instances the peptides were reversible coupled to cTnC. See figure 2.

It was demonstrated that covalent modification of cTnC (C81) with either the peptide or biotin resulted in significant inhibition of activity. See page 248 1st column – Discussion. This data is important to the mechanism of action of hydrophobic anti-CaM drugs that sensitize muscle to Ca^{2+} and potentiate rather than inhibit muscle contraction. A drug with Met-81 would inhibit rather than enhance the function of cTnC. See page 248, 2nd column.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to measure myofilament chemical adducts as taught by Lin et al. in the detection methods of Takahashi et al. in view of Solaro et al. because Lin et al. taught that chemical adduct modifications exhibited inhibition of myofibril activity.

Specifically, the covalent modification of cTnC (C81) with either the peptide or biotin resulted in significant inhibition of activity. See page 248 1st column –Discussion. This data (myofilament chemical adduct modification) is important to the mechanism of action of drug development and utility in muscle contraction (damage/function). See page 248, 2nd column.

Takahashi et al. in view of Solaro et al. and Lin et al. are silent with respect to the myofilament protein modification product being a post-translational modification.

Han et al. teach that post-translational modification involve the making or breaking of covalent bonds. Post-translational modifications are varied. See abstract, page 19-1st column and page 21, for example.

Han et al. further disclose that numerous post-translational modification are recognized in a wide variety of cell types. The covalent changes play several roles in protein-ligand interaction, subcellular organization, assembly of bimolecular complexes, regulation of the catalytic activity, and/or protein turnover. It is well established that each modification severs a useful role…… See page 25-Discussion.

Takahashi et al. in view of Solaro et al. and Lin et al. disclose the claimed method except for specifically indicating that the myofilament modification occurs as a post-translational modification. Han et al. disclose that it is known in the art that protein modification occurs post-translationally and include phosphorylation.

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to detect post-translational modifications, in order to evaluate protein-ligand interaction, subcellular organization, assembly of bimolecular complexes, regulation of the catalytic activity, and/or protein turnover as they relate to muscle damage. See Han et al. page 25-Discussion.

II. Claims 2-7, 28, 34-35, 38 and 40-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takahashi et al. (Clinical Biochemistry, Volume 29, No.4, August 1996, pages 301-308) in view of Solaro et al. (Journal of Molecular Cell Cardiology, Vol.28, pages 217-230, 1996) and Lin et al. (The journal of Biological Chemistry, Vol.271, No.1, 1/5/1996, pages 244-249) and further in view of Han et al. (International Journal of Biochemistry, Vol.24, No.1, 1992, pages 19-28) as applied to claims 1, 16-18, 20-27, and 34 above, and further in view of Wicks et al. (US patent #5,834,220).

Takahashi et al. in view of Solaro et al. and Lin et al. further in view of Han et al. are set forth above.

Takahashi et al. in view of Solaro et al. and Lin et al. further in view of Han et al. differ from the instant invention in not teaching a quantitative (amount) assessment of muscle damage further employing two different myofilament protein modification products.

However, Wicks et al. teach method for assaying for cardiac troponin I along with troponoin C. See abstract. The process and test system provide rapid and specific measurements of troponin I and is highly suitable for confirming the diagnosis of myocardial damage (reading on muscle damage).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to measure two different myofilament product degradation products (troponin I and troponin C) in muscle damage as taught by Wicks et al. in the method of Takahashi et al. in view of Solaro et al. and Lin et al. further in view of Han et al. because Wicks et al. taught that Troponin I is one of three subunits of the troponin complex. The other two subunits (designated T and C) are also immobilized on the thin myofilaments along with troponin I in both cardiac and skeletal muscle tissue. Column 1., lines 23-40. The utility of both troponin I and troponin C allowed for further distinction between cardiac muscle damage or skeletal muscles damage. See column 2, lines 37-49.

One having ordinary skill in the art would have been motivated to do this to acquire the enhanced sensitivity and ability to reduce false positives while providing more data sets for analysis, wherein accurate and precise detection is available.

III. Claims 37 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takahashi et al. (Clinical Biochemistry, Volume 29, No.4, August 1996, pages 301-308) in view of Solaro et al. (Journal of Molecular Cell Cardiology, Vol.28, pages 217-230, 1996) and Lin et al. (The journal of Biological Chemistry, Vol.271, No.1, 1/5/1996, pages 244-249) and further in view of Han et al. (International Journal of Biochemistry, Vol.24, No.1, 1992, pages 19-28) and Wicks et al. (US patent #5,834,220) as applied to claims 2-7, 28, 34-35, 38 and 40-41 above, and further in view of Jideama et al. (The Journal of Biological Chemistry, Vol.271, No.38, 9/20/96, pages 23277-23283).

Please see Takahashi et al. in view of Solaro et al. and Lin et al. further in view of Han et al. and Wicks et al. as set forth above.

Takahashi et al. in view of Solaro et al. and Lin et al. further in view of Han et al. and Wicks et al. differ from the instant invention in not teaching an assessment of the myofilament proteins as a change with time as required in claims 37 and 39.

However, Jideama et al. teach methods to analyze phosphorylation states and properties for myofilament proteins. These myofilament proteins include troponin I and troponin T. The proteins were measured over time (5-120min) –assessing a change with time. Jideama et al found that the phosphorylation state and properties of the myofilament proteins were time dependent relating to phosphorylation extent, substrate affinity, and inhibitions. See page 23278 2nd column –Results through page 23279 and figure 2.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to measure myofilament product degradation products involving phosphorylation states as taught by Jideama et al. in the method of Takahashi et al. in view of Solaro et al. and Lin et al. further in view of Han et al. and Wicks et al. because Jideama et al. taught that the phosphorylation state and properties of myofilament proteins were time dependent relating to phosphorylation extent, substrate affinity, and inhibitions. See page 23278 2nd column –Results through page 23279 and figure 2.

One of skill in the art would have been motivated to measure myofilament products over time in order to evaluate and account for the changes exhibited in phosphorylation extent, substrate affinity, and inhibitions.

Response to Arguments

5. Applicants have amended the claims to read on the measurement of skeletal troponin. Accordingly Takahashi et al. (Clinical Biochemistry, Volume 29, No.4, August 1996, pages 301-308) has been added to the rejections to make the invention obvious.

6. For reasons aforementioned, no claims are allowed.

7. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya, can be reached on (571) 272-0806.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lisa V. Cook
Patent Examiner
Art Unit 1641
Remsen
571-272-0816
8/3/08

/Lisa V. Cook/
Examiner, Art Unit 1641